

Are adjuvant therapies for tonsillectomy evidence based?

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Abstract

Our aim was to ascertain the current practice of adjuvant therapy for tonsillectomy and to determine whether it is evidence based. Anonymized postal questionnaires were sent to all UK otolaryngology consultants registered with the specialty association, and a literature search was performed using relevant search terms in all possible combinations. Among the responders there was little enthusiasm for routine intra-operative local anaesthesia, post-operative topical benzydamine hydrochloride (Difflam) spray or post-operative antibiotics. This is consistent with the lack of robust evidence to support any of these practices. Paracetamol (acetaminophen) is prescribed by almost 90 per cent for post-operative analgesia, and the current literature supports its efficacy and safety. Further, most practitioners combine paracetamol with opioids and/or non-steroidal anti-inflammatory drugs (NSAIDs). Evidence to support the additional use of these agents is, however, non-existent or limited. Some aspects of tonsillectomy care are uniform and evidence based. Others are heterogeneous and suffer from lack of adequate data in the literature.

Key words: Tonsillectomy; Analgesia; Questionnaires; Great Britain

Introduction

Tonsillectomy continues to be one of the commonest surgical procedures performed in the UK, and attracts a significant proportion of the total healthcare expenditure on surgical and post-operative care within the National Health Service (NHS).¹ Tonsillectomy is associated with significant post-operative pain, and is indeed one of the most painful surgical procedures otolaryngologists perform. Adequate analgesia is imperative to minimize pain-associated morbidity, encourage an earlier return to fluid intake and feeding, and to prevent potential complications associated with ineffective pain relief, such as infection. There is a wide spectrum of analgesic drugs currently available, with significant differences in mode of delivery, efficacy, safety and side effects. Numerous studies on adjuvant therapy for tonsillectomy have been published, and various drug regimens have been proposed. However, their impact on what otolaryngologists actually prescribe has not so far been studied.

We undertook a postal questionnaire survey of all otolaryngology consultants in the UK to ascertain their current practice of adjuvant therapy for tonsillectomy. We measured the results of this survey against current best evidence in the literature, to uncover potential areas of concern and controversy.

Methods

A regional pilot study was initially conducted. After the accuracy of data collection and recording had been verified, the final questionnaire was created as a two-page computer-generated sheet. The following questions (with choices illustrated in parentheses) were included: tonsillectomy dissection technique (cold steel, bipolar, co-ablation, laser or other); intra-operative local anaesthesia used (none, pre- or post-incisional, infiltration or topical, lignocaine or bupivacaine and/or epinephrine); and details of routine post-operative analgesia, including the choice of drug(s) (paracetamol (acetaminophen), non-steroidal anti-inflammatory drug (NSAID), opioid, antibiotic and/or benzydamine hydrochloride (Difflam) spray/gargle), duration of prescription (in days), and whether prescribed regularly or rescue only. The responders were also given the option of writing a free text answer. Similar but separate sets of questions for children and adults were produced. The questionnaires were sent by post in April 2003 to all 543 consultant members of the British Association of Otolaryngologists – Head and Neck Surgeons (BAO – HNS) residing in the UK. Data collection was completed in May 2003. The returned forms were scanned by computer, which collated the responses. The data were then entered into a Microsoft Excel spreadsheet for analysis.

TABLE 1

LEVELS OF EVIDENCE (IN DESCENDING ORDER OF PRIORITY)

1.	Cochrane Review
2.	Meta-analysis, systematic review
3.	Randomized controlled study
4.	Non-randomized prospective controlled study
5.	Retrospective controlled study
6.	Case series
7.	Case report
8.	Expert opinion

An electronic English language literature survey of studies on adjuvant care for tonsillectomy was conducted using Medline (1966 to December 2004). For post-operative analgesia, only studies on enteral analgesics were included. The search terms tonsillectomy, local, anaesthesia, analgesia, paracetamol (acetaminophen), codeine, morphine, tramadol, NSAID, haemorrhage, antibiotic, benzydamine hydrochloride (Difflam), pain, duration, rescue and regular were used in all possible combinations in the electronic search. Additional articles, if any, were retrieved by scanning the citations in the articles identified by the electronic search. Levels of evidence used, in descending order of priority, are given in Table 1. The literature search was truncated at the highest available level of evidence, and the results of the postal survey were compared with current best evidence in the literature.

Results

A total of 252 (46.4 per cent) questionnaires were returned. Incomplete, irrelevant and blank responses ($n = 27$) were excluded to give a total of 225 (41.4 per cent) valid responses. Cold steel dissection (51 per cent), bipolar diathermy dissection (36 per cent) and co-ablation (3 per cent) were the preferred techniques of tonsillectomy, with no significant differences in technique between children and adults.

Intraoperative analgesic technique

Only 30 (14 per cent) responders routinely employ intra-operative local anaesthesia (Figure 1). Although it is claimed to provide a pre-emptive analgesic effect,^{2,3} a recent Cochrane Review has concluded that the studies so far have been too small

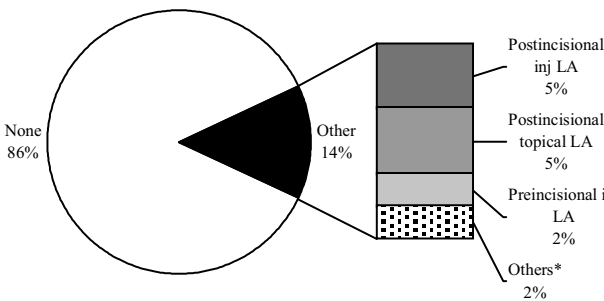


FIG. 1

Intra-operative local anaesthesia.
LA = lignocaine or bupivacaine.

*Epinephrine or epinephrine LA injection.

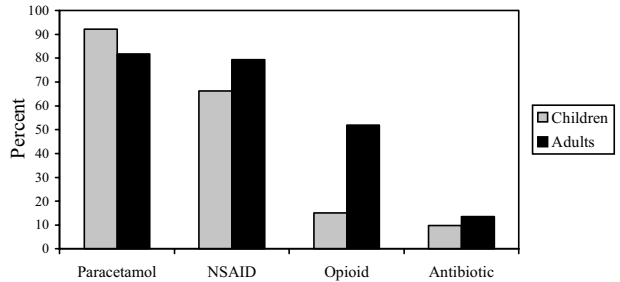


FIG. 2

Post-operative oral analgesics prescribed.

and have failed to show significant benefit.⁴ Furthermore, the agents used in this technique are associated with serious side effects.⁵

Choice of post-operative adjuvant(s)

Figures 2 and 3 illustrate the drugs and combinations used in post-operative analgesia.

Paracetamol. Nearly all responders prefer paracetamol for post-operative analgesia, consistent with several randomized controlled trials emphasizing the relative efficacy and safety of this drug.⁶⁻¹⁰ Only one randomized controlled trial found paracetamol to be inferior to tramadol (opioid) for pain relief.¹¹ In this trial, however, the dose of paracetamol used was lower than the recommended dosage.

Additional adjuvants

In addition to paracetamol, most of our responders prefer opioids and/or NSAIDs (ibuprofen in children and diclofenac in adults) for post-operative analgesia (Figures 2 and 3). However, evidence to support their additional use is non-existent or limited.

Opioid. There is a paucity of studies comparing the opioid-paracetamol combination versus paracetamol following tonsillectomy. Only Moir *et al.* have addressed this issue in a randomized controlled trial, and they found the regimen to be equianalgesic.⁷ Further, opioids are associated with sedation and gastrointestinal side effects.

NSAIDs. There is no study comparing NSAIDs-paracetamol with paracetamol alone.

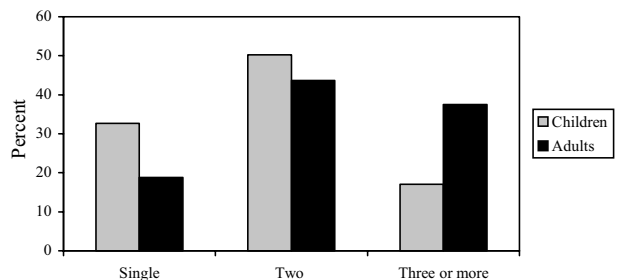


FIG. 3

Number of oral analgesics prescribed as part of the post-operative regimen.

TABLE II
EFFICACY OF NSAIDS VS. PARACETAMOL AND/OR OPOID* (ALL STUDIES RANDOMIZED CONTROLLED)

Study	n	NSAID	Comparison group	Conclusion
1. Courtney & Cabraal ¹²	64	Diclofenac	tramadol	NSAID equivalent
2. Harley <i>et al.</i> ¹³	27	Ibuprofen	paracetamol + codeine	NSAID inferior
3. St Charles <i>et al.</i> ¹⁴	110	Ibuprofen	paracetamol + codeine	NSAID equivalent
4. Pasquale <i>et al.</i> ¹⁵	35	Nimuselide	paracetamol	NSAID equivalent
5. Parker <i>et al.</i> ¹⁶	77	Ibuprofen	placebo	NSAID superior
6. Dommerby ¹⁷	97	Diclofenac	placebo	NSAID superior

* Studies on enteral analgesia only included.
n = total number of patients.

Although NSAIDs have been established to be superior to placebo, they have been found to be no more efficacious than paracetamol and/or opioids (Table 2).

The risk of post-operative haemorrhage with NSAIDs, which are potent inhibitors of platelet aggregation, has been analysed in three separate meta-analyses.^{18–20} Table 3 is culled from these meta-analyses and illustrates all randomized controlled trials comparing post-operative enteral NSAIDs with an enteral control drug. All documented post-operative haemorrhages are presented in the data. The pooled odds ratio of 0.98 for NSAIDs does not suggest a higher bleeding risk with these agents.

Antibiotic. Unlike in the United States, where antibiotics are routinely used in the post-operative period,⁵ only a small proportion of clinicians prescribe them in the UK (13.5 per cent in adults and 10 per cent in children; Figure 2). Only five randomized controlled trials so far have investigated the role of oral antibiotics, and the results are mixed (Table 4).

Benzydamine hydrochloride (Difflam) spray. Ancillary post-operative measures such as topical benzydamine hydrochloride (Difflam) gargle/spray are prescribed in only 23 per cent of adults and 4.4 per cent of children. This is entirely consistent with the lack of evidence in the literature to support their use. Two randomized controlled trials so far have compared topical benzydamine hydrochloride with placebo. One found no benefit,²⁶ but the other reported improved pain control and better swallowing on post-operative day two.²⁷

Regular vs rescue analgesia

Most responders prescribe post-operative analgesia

on a regular basis, whereas 25 per cent prefer rescue-only pain relief (Figure 4). Only two trials so far have compared regular versus rescue analgesia following tonsillectomy, and the results are conflicting. The earlier trial (non-randomized controlled) found regular analgesia to be more efficacious (better pain control and earlier return to solid feeds),²⁸ whereas a more recent (randomized controlled) trial found no significant benefit with a regular regimen.²⁹

Duration of post-operative analgesia

Approximately 65 per cent of responders prescribe post-operative analgesia for seven days or less (Figure 5). Although the duration of post-tonsillectomy pain can show considerable individual variation, several studies document significant pain lasting beyond the first week.^{30–33} Others estimate such pain to last for an average of 8–11 days.^{27,34} Salonen and Kokki³⁴ also estimate the average duration of analgesic consumption to be 12 days. Given these data, the current practice of analgesic prescription for seven days or less among our respondents is probably inadequate.

There was no statistical difference in the duration of post-operative analgesics prescribed for adults versus children (Figure 5; $p = 0.256$ by normal distribution for means). However, in the literature, post-operative pain in children is reported to resolve faster than in adults.³⁵

Discussion

Despite being an area of high-volume high-priority practice in otolaryngology, adjuvant care after tonsillectomy is not uniform among our responders. There is consensus on some aspects of care, and diversity on others. The latter is chiefly attributable to the lack of robust data in the literature. Well-

TABLE III
RISK OF HAEMORRHAGE* WITH ENTERAL NSAIDS (ALL STUDIES RANDOMIZED CONTROLLED)

Study	NSAID	Comparison group	Incidence of haemorrhage		OR (95% CI)
			NSAID	Control	
1. Courtney <i>et al.</i> ¹²	Diclofenac	Tramadol	6/25	7/24	0.77 (0.22–2.71)
2. Harley <i>et al.</i> ¹³	Ibuprofen	Paracetamol + codeine	2/16	0/11	5.78 (0.33–103)
3. St Charles <i>et al.</i> ¹⁴	Ibuprofen	Paracetamol + codeine	4/55	5/55	0.79 (0.20–3.06)
4. Dommerby ¹⁷	Diclofenac	Placebo	5/47	4/50	1.36 (0.35–5.34)
5. Pasquale <i>et al.</i> ¹⁵	Nimuselide	Paracetamol	0/16	0/19	n/a
6. Parker <i>et al.</i> ¹⁶	Ibuprofen	Placebo	0/44	0/33	n/a
Pooled odds ratio			17/203	16/192	0.98

* Any documented post-operative haemorrhage.
OR = odds ratio; CI = Confidence interval.

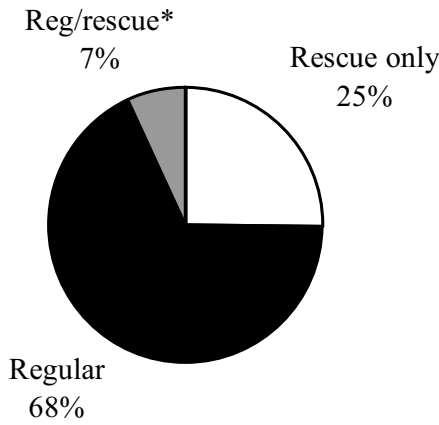


FIG. 4

Regular or rescue analgesia.
 *Regular initially followed by rescue.

designed studies on adjuvant therapy for tonsillectomy are few, use varying methodologies and end-points, focus on peri-operative care to the relative exclusion of longer term post-operative pain relief, and often arrive at conflicting results.

There is little enthusiasm for intra-operative local anaesthesia, post-operative topical benzydamine hydrochloride (Difflam) spray or post-operative antibiotics. This is consistent with the lack of robust evidence to support any of these practices. Further, any putative benefit of antibiotics has to be carefully weighed against the possible emergence of resistant bacteria, fungal infection, and the risk of adverse events.

Paracetamol is justifiably the most popular post-operative analgesic. In addition, most prefer opioids and/or NSAIDs. This theoretically enhances efficacy, by combining two drugs with different mechanisms of action, and also allows for a reduction of their individual doses, thereby minimizing side effects. An enhanced efficacy effect has been reported for such combination therapy following non-otolaryngological procedures such as laparotomy.³⁶ However, evidence to support such combined therapy following tonsillectomy is non-existent or limited. It is also unknown whether spacing the additional adjuvant in between paracetamol doses improves analgesia. Enteral NSAIDs have been shown not to incur a higher risk of post-operative bleeding. Nevertheless, current data are few and more trials are needed to establish conclusively the safety of this drug.

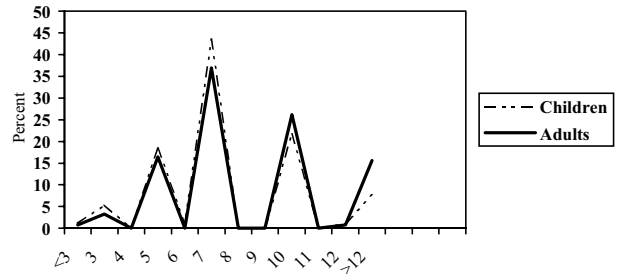


FIG. 5

Duration of post-operative analgesia.

It is logical to assume that regular, as opposed to rescue-only, post-operative analgesia is better for pain control, because it sustains drug concentration largely within the therapeutic range, whereas rescue-only doses may result in deep troughs in serum levels and significant ‘breakthrough’ pain.³⁷ Evidence to support a regular regimen following tonsillectomy is, however, scant, and further trials are needed. As significant post-operative pain can potentially last for more than seven days, patients need to be appropriately warned and told about the need for adequate analgesia until the resolution of pain and resumption of normal diet.

We acknowledge several limitations in the present report. First, the response rate of 41.4 per cent may be insufficient to accurately reflect contemporary practice, but may represent a current ceiling for similar national surveys.³⁸ Preference for a particular adjuvant therapy, however, has negligible influence on the response rate of an anonymized survey, and it is reasonable to assume that the adjuvant regimen of non-responders will not be significantly different from that of the responders. Second, current best evidence has been mostly presented *de facto*. No systematic review or meta-analysis has been attempted, as neither is within the scope of the present review. Lastly, this report focuses on adjuvant therapy as practised by surgeons, and largely ignores other aspects of peri-operative care, such as parenteral analgesics/adjuvants, which fall under the purview of anaesthetists. The effect of such peri-operative adjuvants is, however, restricted to the immediate post-operative period, with little impact on surgeon-controlled, longer-term post-operative care.

Aforementioned limitations notwithstanding, this report is significant for two reasons: areas of consensus and diversity in contemporary practice have been uncovered; and areas with a robust as well as those with a poor evidence base have been

TABLE IV
 BENEFIT OF ANTIBIOTIC* (ALL STUDIES RANDOMIZED CONTROLLED)

Study	n	Antibiotic	Effect of antibiotic
1. O’Reilly <i>et al.</i> ²¹	95	Amoxicillin	No benefit
2. Mann <i>et al.</i> ²²	18	Amoxicillin	No benefit
3. Colreavy <i>et al.</i> ²³	78	Amoxicillin + clavulanate	Less analgesic consumed, less time to resume normal diet and pain scores
4. Grandis <i>et al.</i> ²⁴	101	Amoxillicin + clavulanate	Less mouth odour, earlier return to normal diet and activities
5. Telian <i>et al.</i> ²⁵	85	Amoxicillin	Less mouth odour, fever, number of days in pain and earlier return to normal diet and activities

* Control group – no antibiotic
 n = total number of patients.

illustrated. The former will serve as a reference point for comparison with peer practice, and the latter will serve as a guide for evidence-based medicine. Both will be important to the practising otolaryngologist when making informed decisions regarding the care of the tonsillectomy patient.

- **The current practice of adjuvant therapies for tonsillectomy and whether they are evidence based have not been previously ascertained**
- **Among British otolaryngologists there is little enthusiasm for intra-operative local anaesthesia, post-operative topical benzydamine hydrochloride spray or post-operative antibiotics, consistent with the lack of robust evidence to support any of these practices**
- **Paracetamol is the most preferred post-operative analgesic, with current evidence supporting its efficacy and safety**
- **Evidence to support the additional use of opioid or non-steroidal anti-inflammatory drugs (NSAIDs) is non-existent or limited**

Conclusion

Some aspects of tonsillectomy care are uniform and evidence based. Others are varied, and suffer from lack of adequate data in the literature. In the latter instance, practice appears to be influenced by 'conventional wisdom', anecdotal evidence and individual/institutional experience, preferences and guidelines. Although paracetamol is justifiably the most popular post-operative analgesic, it is often combined with opioids and/or NSAIDs, for a theoretically better analgesia. However, any such added beneficial effect remains to be proven. Side effects and adverse events also need to be carefully considered before additional adjuvants are prescribed. Further well-designed trials are called for to address aspects of tonsillectomy care with a limited evidence base.

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